UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,808	12/19/2001	Thomas D. Meek	P51217	6102

7590 11/26/2003

Edward R. Gimmi
SmithKline Beecham Corporation
Corporate Intellectual Property-U.S., UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939

EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	4

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/024,808	Applicant(s) MEEK ET AL.	
	Examiner Patricia A. Duffy	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1, 9, 10 and 2-8 and 11-17 (in part)* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8 and 11-17 (in part)* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-17* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The response filed 7-10-03 has been entered into the record.

Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/259,595 filed January 3, 2001. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which

the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 2-8 and 11-17 of this application, see rejections under 35 USC 112 below.

Information Disclosure Statement

The information disclosure statements filed March 25, 2002 and April 12 2002 have been considered. Initialed copies are enclosed.

Election/Restrictions

Applicant's election with traverse of Group III and the specie "a conformational change upon acetoacetyl-CoA binding resulting in formation of an LBHB between Tyr 157 and Lys 161" in Paper No. 10 is acknowledged. The response provided no actual traversal of the restriction requirement.

The requirement is therefore still deemed proper and is therefore made FINAL.

Claims 1, 9, 10, 2-8 (in part), and 11-17 (in part) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-8 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to methods of the treatment of an individual having the need to inhibit FabG polypeptide comprising administering to an individual an antibacterially effective amount of an antagonists that inhibits an activity of a polypeptide having SEQ ID NO:2 or is at least 90% identical with SEQ ID NO:2 wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161; or methods of inhibiting an activity of FabG wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161; and methods of inhibiting the growth of a bacteria by administering an antibacterially effective amount of an antagonists that inhibits an activity of a polypeptide having SEQ ID NO:2 or is at least 90% identical with SEQ ID NO:2 wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161.

The specification fails to provide a written description of any antagonist structure that inhibits any activity of FabG, SEQ ID NO:2 or 90% identical variant of SEQ ID NO:2 wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161. No structural characteristics are provided, nor its there any indication that Applicants had possession of any antagonist or any antagonist that functioned as claimed. The specification fails to provide the structural requirements of members of a genus that functions to inhibit a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161. This situation is analogous to that of *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1389 (Fed. Cir. 1997). Additionally, Price et al (Biochemistry, 40:12772-12781, 2001) teach that FabG is the only known isozyme to catalyze reduction of the beta-Keto group and that it is an essential enzyme in bacteria and an ideal target for the development of new antibiotics. Price et al also teaches that FabG is not targeted by any known inhibitors (i.e. the instant antagonist; see page 12772, column 2, second paragraph, last sentence). Because one skilled in the art would clearly conclude that the inventors were not in possession of the claimed invention the claims fail to comply with the written description requirement.

Claim 2-8 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to methods of the treatment of an individual having the need to inhibit FabG polypeptide comprising administering to an individual an antibacterially effective amount of an antagonists that inhibits an activity of a polypeptide having SEQ ID NO:2 or is at least 90% identical with SEQ ID NO:2 wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161; or methods of inhibiting an activity of FabG wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161; and methods of inhibiting the growth of a bacteria by administering an antibacterially effective amount of an antagonists that inhibits an activity of a polypeptide having SEQ ID NO:2 or is at least 90% identical with SEQ ID NO:2 wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161.

The specification is not enable to perform the claimed methods using any antagonist with the function of inhibiting an activity of FabG wherein the activity is a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 because it fails to disclose ~~and~~ particular structure for the antagonist used in the claimed methods. The specification does not

provide any guidance or any working examples in this unpredictable are, and thus the skilled artisan would have been unable to prepare the claimed antagonist for use the claimed methods. There are no starting materials provided, no method steps, no references to known processes, no final product tested and no correlation between a particular antagonist structure and the claimed activity that the antagonist structure must have. Furthermore, an assay for finding a product, absent further information, is not equivalent to a positive recitation of how to make a product with specific inhibitory requirements. Therefore, this claims fails to been the enablement requirement for the "how to make" and antagonist that functions as claimed in order to use it in the method as claimed. Furthermore, the success of state of the art structure-based strategies for inhibitor design is highly unpredictable. For example, Kuntz, (Science 257:1078-1031, 1992; 1449) on page 1080, column 3, discloses that as little as 2% of compounds predicted to inhibit specific enzymatic or receptor systems actually show inhibition in the micromolar range. Kuntz further discloses that "optimization" of these compounds has proven even more problematic. The resolution of structure of proteins and peptides are exceedingly labor-intense, and success is unpredictable. Therefore, in view of the unpredictability in the art, and in view of the insufficient guidance and working examples in the specification, the quantity of experimentation required by one skilled in the art to practice the invention undue. In the absence of a further guidance, it would require undue

experimentation to make antagonists that function as claimed for use in the methods of treatment, inhibiting FabG and inhibiting bacterial growth.

Claims 2-8 and 11-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 2-8 and 11-17, the claims are confusing because they include non-elected subject material.

As to claims 2-8, and 14-17, the claims are rendered indefinite from the use of the term "antibacterially effective amount" because it is unclear how this relates to the claimed antagonist activity of a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161 and no connection between this term and the goal of the preamble.

As to claim 12, the claim is indefinite because it is a method with no positively recited active method steps.

As to claims 2-8 and 11-17, the claims are prima facie indefinite in the recitation of the acronym "fabG" without specific claimed identifying information.

As to claims 5-8 and 11-17, the recitation of Tyr157 and Lys161 is indefinite in the absence of any sequence identifier because they are relative positions within a complete

open reading frame and the claims do not provide a such a reference and therefore one of skill in the art would not be able to determine the correct Tyr and the corresponding Lys.

As to claims 2-4, the 90% identical variants are not required to posses Tyr157 and Lys161 as critical positions, therefore the examined activity requirement renders the claims confusing.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

Claims 2-8 and 11-17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Huang et al (U.S. Patent No. 6,110,704, issued August 29, 2000).

Huang et al contemplates antagonists of fabG (3-ketoacyl-acyl carrier protein reductase) of *Staphylococcus aureus* and use of the antagonists for treating bacterial infections and conditions associated with such infections (column 2, lines 22-26). Huang et al teach that those compounds that are bacteriostatic and/or bactericidal are of particular benefit (see column 18, lines 40-45). Because, the instantly claimed function of a conformational change upon acetoacetyl-CoA binding resulting in formation of a low

barrier hydrogen bond (LBHB) between Tyr157 and Lys161 is critical to enzymatic activity (i.e. binding of AcAc-CoA to fabG; see Figure 4 and 5 of the instant specification); inhibitors of activity in general (antagonists) necessarily have the functional activity of inhibiting a conformational change upon acetoacetyl-CoA binding resulting in formation of a low barrier hydrogen bond (LBHB) between Tyr157 and Lys161. Huang et al contemplates antagonists of fabG that are bactericidal or bacteriostatic.

Therefore, the methods and antagonists of fabG and variants of Huang et al meet the limitation of the claims.

Status of the Claims

Claims 2-8 and 11-17 (in part) stand rejected. Claims 1, 9 and 10 and claims 2-8 and 11-17 (in part) are withdrawn from consideration.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 703-305-7555. The examiner can normally be reached on M-F 9:30pm-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on 703-308-3909. The fax phone numbers for

the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645

Patricia A. Duffy, Ph.D.
November 25, 2003